

28. (Amended) The non-human transgenic mammal of claim 27 wherein the altered lysostaphin gene comprises an alteration that disrupts one or more mammalian post-translational processing events.

29. (Amended) The non-human transgenic mammal of claim 28 wherein the transgene contains nucleotide sequences as in SEQ ID NO: 3, which comprises in operable association:

a eukaryotic mammary specific promoter located 5' to the transgene;

a eukaryotic start codon located 3' to the eukaryotic promoter;;

a Kozak expression start site consensus sequence located 3' to the eukaryotic promoter and including the eukaryotic start codon;

a eukaryotic secretion signal located 3' to the Kozak expression start site; and

a coding sequence located 3' to the secretion signal, wherein coding sequence encodes the lysostaphin protein which lysostaphin protein has an amino acid sequence that differs from a naturally-occurring lysostaphin protein in that at least one glycosylation site have been removed in expression of the lysostaphin protein in mammary cells and tissues.

30. (Amended) The non-human transgenic mammal of claim 27 wherein the transgene contains nucleotide sequences as in SEQ ID NO: 3, which comprises in operable association:

a eukaryotic mammary specific promoter located 5' to the transgene;

a eukaryotic start codon located 3' to the eukaryotic promoter;

a Kozak expression start site consensus sequence located 3' to the eukaryotic promoter and including the eukaryotic start codon; and

a coding sequence located 3' to the Kozak expression start site, which coding sequence encodes the lysostaphin protein, which lysostaphin protein has an amino acid sequence that differs from a naturally-occurring lysostaphin protein in that at least one glycosylation site is removed, wherein the operable association expression of the lysostaphin protein in mammary cells and tissues.

31. (Amended) The non-human transgenic mammal of claim 27 or 28 wherein the transgene is inserted into a bovine β -lactoglobulin expression cassette which comprises:

a nucleic acid sequence encoding 4.2 kilobase pairs of the 5'-regulatory region of the bovine β -lactoglobulin gene;

a nucleic acid sequence encoding exons 5, 6, and 7 of the bovine β -lactoglobulin gene; and

a nucleic acid sequence encoding 2.0 kilobases of 3'-untranslated region of the bovine β -lactoglobulin gene, wherein the 5'-regulatory region is located upstream of exons 5, 6, and 7, and exons 5, 6, and 7 are located upstream of the 3'-untranslated region, wherein the insertion of the altered lysostaphin transgene into the β -lactoglobulin expression cassette results in expression of the lysostaphin transgene in mammary cells and tissues.

32. (Amended) A non-human transgenic mammal that comprises a transgene including an altered non-mammalian anti-microbial gene, which altered non-mammalian anti-microbial gene differs from a naturally-occurring non-mammalian anti-microbial gene in that the altered non-mammalian anti-microbial gene contains one or more sequences necessary and sufficient for expression of an active secreted non-mammalian anti-microbial protein by mammalian cells and tissues.

33. (Amended) The non-human transgenic mammal of claim 32 wherein the alteration to the non-mammalian anti-microbial transgene is an alteration that disrupts one or more mammalian post-translational processing events.

34. (Amended) The non-human transgenic mammal of claim 32 wherein the non-mammalian anti-microbial transgene comprises in operable association:

a eukaryotic mammary specific promoter located 5' to the transgene;

a eukaryotic start codon located 3' to the eukaryotic promoter;

a Kozak expression start site consensus sequence located 3' to the eukaryotic promoter and including the eukaryotic start codon;

a eukaryotic secretion signal located 3' to the Kozak expression start site; and

a nucleic acid sequence located 3' to the secretion signal, the nucleic acid sequence encoding the non-mammalian anti-microbial polypeptide from which at least one glycosylation site in the non-mammalian anti-microbial polypeptide is removed, wherein the operable association polypeptide results in expression of the non-mammalian anti-microbial polypeptide in mammary cells and tissues.

35. (Amended) The non-human transgenic mammal of claim 37 wherein the non-mammalian anti-microbial transgene encoding the non-mammalian anti-microbial protein is modified to comprise in operable association:

a eukaryotic mammary specific promoter located 5' to the transgene;

a eukaryotic start codon located 3' to the eukaryotic promoter;

a Kozak expression start site consensus sequence located 3' to the eukaryotic promoter and including the eukaryotic start codon; and;

a nucleic acid sequence located 3' to the Kozak expression start site, the nucleic acid sequence encoding the non-mammalian anti-microbial polypeptide from which at least one glycosylation site in the non-mammalian anti-microbial polypeptide is removed, wherein the operable association results in expression of the non-mammalian anti-microbial polypeptide in mammary cells and tissues.

36. (Amended) The non-human transgenic mammal of claim 32 or 33 wherein the altered non-mammalian anti-microbial transgene is inserted into a bovine β -lactoglobulin expression cassette which comprises:

a nucleic acid sequence encoding 4.2 kilobase pairs of the 5'-regulatory region of the bovine β -lactoglobulin gene;

a nucleic acid sequence encoding exons 5, 6, and 7 of the bovine β -lactoglobulin gene;
and

a nucleic acid sequence encoding 2.0 kilobases of 3'-untranslated region of the bovine β -lactoglobulin gene,

a wherein in the β -lactoglobulin expression cassette the 5'-regulatory region of the bovine- β -lactoglobulin gene is located upstream of exons 5, 6, and 7, and exons 5, 6, and 7 are located upstream of the 3'-untranslated region, wherein the insertion of the altered transgene into the β -lactoglobulin expression cassette results in expression of the transgene in mammary cells and tissues.

Please add the following new claims.

37. (New) The non-human transgenic mammal of claim 27 or 32, wherein the alteration to the lysostaphin transgene is an alteration that adds or removes one or more mammalian post-translational processing sites.
38. (New) The non-human transgenic mammal of claim 28 or 33, wherein the alteration comprises a disruption of at least one glycosylation site.
39. (New) The non-human transgenic mammal of claim 27 or 32, wherein the mammalian cells and tissues comprise mammary cells and tissues.
40. (New) The non-human transgenic mammal of claim 39, wherein the mammary cells and tissues comprise mammary secretory cells and tissues.
41. (New) The non-human transgenic mammal of claim 32, wherein the non-mammalian anti-microbial gene encodes an anti-viral peptide or protein.
42. (New) The non-human transgenic mammal of claim 32, wherein the non-mammalian anti-microbial gene encodes a microbial peptide or protein.
43. (New) The non-human transgenic mammal of claim 32, wherein the non-mammalian anti-microbial gene encodes a prokaryotic peptide or protein.
44. (New) The non-human transgenic mammal of claim 32, wherein the non-mammalian anti-microbial gene encodes a bacterial peptide or protein.

45. (New) The non-human transgenic mammal of claim 32, wherein the non-mammalian anti-microbial is selected from the group consisting of nisins, muramidases, glucoasminidases, endopeptidases, and colicins.

46. (New) The non-human transgenic mammal of claim 32, wherein the non-mammalian anti-microbial is an anti-staphylococcal.

47. (New) The non-human transgenic mammal of claim 46, wherein the anti-staphylococcal is selected from the group consisting of β -lytic protease, lysostaphin, α -lytic protease, lyt-M, at 1ALE-1, and zooA.

48. (New) The non-human transgenic mammal of claim 46, wherein the anti-staphylococcal is β -lytic protease.

49. (New) The non-human transgenic mammal of claim 46, wherein the anti-staphylococcal is lysostaphin.

50. (New) A non-human transgenic mammal comprising a transgene encoding a non-mammalian anti-microbial protein, wherein the transgene comprises a nucleic acid sequence encoding the non-mammalian anti-microbial protein operatively linked to a tissue-specific promoter sufficient to direct expression of the non-mammalian antimicrobial protein in mammalian cells and tissues, wherein the nucleic acid sequence encoding the non-mammalian anti-microbial protein is modified such that at least one glycosylation site in the non-mammalian anti-microbial protein coding sequence is disrupted.

51. (New) The non-human transgenic mammal of claim 50, wherein the transgene encoding the non-mammalian anti-microbial protein is further operatively linked to a sequence encoding a signal peptide such that the lysostaphin polypeptide is secreted.

52. (New) The non-human transgenic mammal of claim 50, wherein the non-mammalian anti-microbial gene encodes an anti-viral peptide or protein.

53. (New) The non-human transgenic mammal of claim 50, wherein the non-mammalian anti-microbial gene encodes a microbial peptide or protein.

54. (New) The non-human transgenic mammal of claim 50, wherein the non-mammalian anti-microbial gene encodes a prokaryotic peptide or protein.

55. (New) The non-human transgenic mammal of claim 50, wherein the non-mammalian anti-microbial gene encodes a bacterial peptide or protein.

56. (New) The non-human transgenic mammal of claim 50, wherein the non-mammalian anti-microbial is selected from the group consisting of nisins, muramidases, glucoasminidases, endopeptidases, and colicins.

57. (New) The non-human transgenic mammal of claim 50, wherein the non-mammalian anti-microbial is an anti-staphylococcal.

58. (New) The non-human transgenic mammal of claim 57, wherein the anti-staphylococcal is selected from the group consisting of β -lytic protease, lysostaphin, α -lytic protease, lyt-M, at 1ALE-1, and zooA.

59. (New) The non-human transgenic mammal of claim 57, wherein the anti-staphylococcal is β -lytic protease.

60. (New) The non-human transgenic mammal of claim 57, wherein the anti-staphylococcal is lysostaphin.

61. (New) A non-human transgenic mammal comprising a transgene encoding lysostaphin, wherein the transgene comprises a nucleic acid sequence encoding lysostaphin operatively linked to at least one mammary expression signal sufficient to direct expression of lysostaphin in mammary cells and tissues, wherein the nucleic acid sequence encoding lysostaphin is modified such that at least one glycosylation site in the lysostaphin coding sequence is disrupted.

62. (New) The non-human transgenic mammal of claim 61, wherein the lysostaphin coding sequence is further operatively linked to a sequence encoding a signal peptide such that the lysostaphin polypeptide is secreted from the mammalian cells.

63. (New) The non-human transgenic mammal of claim 61, wherein two glycosylation sites are modified.